AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning on page 8, line 33 through page 9, line 5, with the following:

Certain embodiments of the invention use a pharmaceutical formulation for the slow prolonged release of interleukin(s) in vivo, this formulation being an aqueous colloidal suspension of low viscosity comprising submicronic particles of polymer PO that are auto-associated with at least one interleukin, the polymer PO being e.g. a polyamino acid formed of aspartic units and/or glutamic units, at least some of these units carrying grafts containing at least one hydrophobic group ~~[(HG)]~~[GH], PO also being biodegradable, water-soluble and amphiphilic.

Please replace the paragraph beginning on page 9, lines 15-35, with the following:

The invention thus relates to a liquid pharmaceutical formulation for the prolonged release of interleukin(s), this formulation comprising an aqueous colloidal suspension of low viscosity based on submicronic particles of water-soluble biodegradable polymer (PO) carrying hydrophobic groups ~~[(HG)]~~[GH], said particles being non-covalently associated with at least one interleukin and optionally with at least one active principle (AP), characterized in that:

- the dispersion medium of the suspension consists essentially of water,
- said formulation is capable of being injected parenterally and then forming a gelled deposit *in vivo*, this formation of a gelled deposit:
  - on the one hand being at least partly caused by at least one physiological protein present *in vivo*,
  - and on the other hand making it possible to prolong and control the *in vivo* release time of the AP beyond 24 h after administration,

- it is liquid under the injection conditions,
- and it is also liquid at the physiological temperature and/or physiological pH and/or in the presence of:
  - a physiological electrolyte in a physiological concentration,
  - and/or at least one surfactant.

Advantageously, this gelling *in vivo* does not result from a change in pH and/or temperature or from the dispersion *in vivo* of one or more organic solvents that may be present in the injected formulation.

Please replace the paragraph beginning on page 10 lines 7-23, with the following:

According to one mode of definition, which is based not on an *in vivo* behaviour, as indicated above, but on an *in vitro* behaviour, the invention relates to a liquid pharmaceutical formulation for the prolonged release of interleukin(s) and optionally other active principle(s) (AP), this formulation:

- being liquid in the ambient atmosphere,
- also being liquid at the physiological temperature and/or physiological pH and/or in the presence of:
  - a physiological electrolyte in a physiological concentration,
  - and/or at least one surfactant,
- and comprising an aqueous colloidal suspension of low viscosity based on submicronic particles of water-soluble biodegradable polymer PO carrying hydrophobic groups ~~HG~~GH, said particles being non-covalently associated with at least one interleukin (and optionally at least one other active principle), and the dispersion medium of the suspension consisting essentially of water,

characterized in that its concentration of [PO] is set at a sufficiently high value to allow the formation of a gelled deposit in vitro after parenteral injection, in the presence of at least one protein.

Please replace the paragraph beginning on page 14, lines 13-18, with the following:

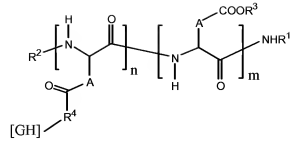
The polymers PO according to the invention are water-soluble biodegradable polymers carrying hydrophobic groups ~~H~~GGH. The hydrophobic groups can be in reduced number relative to the rest of the chain and can be attached laterally to the chain or intercalated in the chain and be distributed randomly (random copolymer) or distributed in the form of sequences or grafts (block copolymers or sequenced copolymers).

Please replace the paragraph beginning on page 15, lines 2-6, with the following:

In one particularly preferred embodiment of the invention, the polymer PO is a polyamino acid formed of aspartic units and/or glutamic units, at least some of these units carrying grafts containing at least one hydrophobic group ~~H~~GGH. These polyamino acids are especially of the type described in PCT application WO-A-00/30618.

Please replace the paragraph beginning on page 15, line 7 through page 16, line 8, with the following:

According to a first possibility, the PO of the formulation is (are) defined by general formula **(I)** below:



(I)

in which:

- R^1 is H, a linear C2 to C10 alkyl or branched C3 to C10 alkyl, benzyl, a terminal amino acid unit or -R^4-~~[HG]~~[GH];
- R^2 is H, a linear C2 to C10 acyl or branched C3 to C10 acyl group, a pyroglutamate or -R^4-~~[HG]~~ [GH];
- R^3 is H or a cationic entity preferably selected from the group comprising:
  - metal cations advantageously selected from the subgroup comprising sodium, potassium, calcium and magnesium,
  - organic cations advantageously selected from the subgroup comprising:
    - cations based on amine,
    - cations based on oligoamine,
    - cations based on polyamine (polyethylenimine being particularly preferred),
    - cations based on amino acid(s) advantageously selected from the class comprising cations based on lysine or arginine,

- and cationic polyamino acids advantageously selected from the subgroup comprising polylysine and oligolysine;

- R^4 is a direct bond or a "spacer" based on 1 to 4 amino acid units;

- A independently is a radical $-CH_2-$ (aspartic unit) or $-CH_2-CH_2-$ (glutamic unit);

- n/(n + m) is defined as the molar grafting rate and its value is sufficiently low for PO, dissolved in water at pH 7 and at 25°C, to form a colloidal suspension of submicronic particles of PO, n/(n + m) preferably being between 1 and 25 mol% and particularly preferably between 1 and 15 mol%;

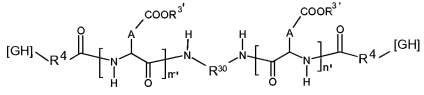
- n + m is defined as the degree of polymerization and varies from 10 to 1000 and preferably between 50 and 300;

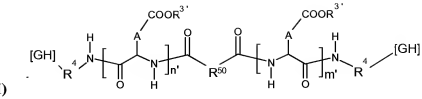
- ~~HG~~GH is a hydrophobic group.

Please replace the paragraph beginning on page 16, line 9 through page 17, line 11, with the following:

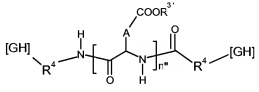
According to a second possibility, the PO of the formulation has (have) one of general formulae **(II), (III)** and **(IV)** below:

(**II**)





(III)



(IV)

in which:

- ~~HG~~GH is a hydrophobic group;
- R^{30} is a linear C2 to C6 alkyl group;
- $R^{3'}$ is H or a cationic entity preferably selected from the group comprising:
  - metal cations advantageously selected from the subgroup comprising sodium, potassium, calcium and magnesium,
  - organic cations advantageously selected from the subgroup comprising:
    - cations based on amine,
    - cations based on oligoamine,
    - cations based on polyamine (polyethylenimine being particularly preferred),
    - cations based on amino acid(s) advantageously selected from the class comprising cations based on lysine or arginine,

- and cationic polyamino acids advantageously selected from the subgroup comprising polylysine and oligolysine;

- R^{50} is a C2 to C6 alkyl, dialkoxy or diamine group;

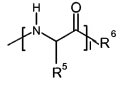
- R^4 is a direct bond or a "spacer" based on 1 to 4 amino acid units;

- A independently is a radical $-CH_2-$ (aspartic unit) or $-CH_2-CH_2-$ (glutamic unit);

- n′ + m′ or n″ is defined as the degree of polymerization and varies from 10 to 1000 and preferably between 50 and 300.

Please replace the paragraph beginning on page 17, line 12 through page 18, line 2, with the following:

Advantageously, the n ~~HG~~GH groups of the PO each independently of one another are a monovalent radical of the formula below:



~~(HG)~~(GH)

in which:

- R^5 is a methyl (alanine), isopropyl (valine), isobutyl (leucine), sec-butyl (isoleucine) or benzyl (phenylalanine);

- R^6 is a hydrophobic radical containing from 6 to 30 carbon atoms;

- l varies from 0 to 6.

According to one noteworthy characteristic of the invention, all or some of the hydrophobic groups R^6 of the PO are independently selected from the group of radicals comprising:

- a linear or branched alkoxy containing from 6 to 30 carbon atoms and optionally containing at least one heteroatom (preferably O and/or N and/or S) and/or at least one unit of unsaturation,
- an alkoxy containing 6 to 30 carbon atoms, having one or more fused carbocyclic rings and optionally containing at least one unit of unsaturation and/or at least one heteroatom (preferably O and/or N and/or S),
- an alkoxyaryl or an aryloxyalkyl having 7 to 30 carbon atoms and optionally containing at least one unit of unsaturation and/or at least one heteroatom (preferably O and/or N and/or S).